| **Document no.:** | **Effective Date:** | **Version:** 1 |
|---|---|---|
| **Author:** Karl Firth | **Approver:** | **Reviewer:** |



| Revision History | |
|---|---|
| Major version | Overall description of change |
| 1.0 | Initial version. |
| 2.0 | |
| 3.0 | |
| | |

# STATISTICAL ANALYSIS PLAN

**27th March, 2023**

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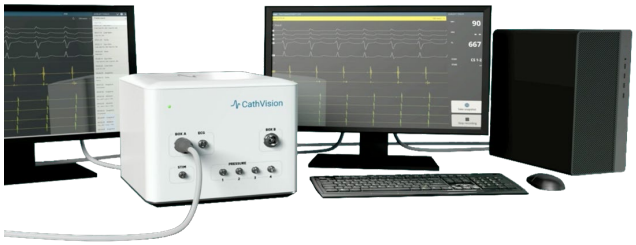
## STUDY SYNOPSIS

| | |
|---|---|
| **Title** | A Prospective, Multi-Center, Open-Label, Single-Arm Study to Evaluate the Safety and Technical Performance of the CathVision ECGenius® System |
| **Investigational device** | The CathVision ECGenius® System is an electrophysiology (EP) recording system to be used in EP studies as a tool to monitor, display, and record signals of the heart and cardiac arrhythmias.<br>  |
| **Intended Use** | To acquire, amplify, digitize, stream atrial and ventricular intracardiac electrophysiology signals during cardiac electrophysiology studies and related procedures. |
| **Objective** | The primary objective is to evaluate the safety and technical performance of the CathVision ECGenius® System. The secondary objective is to benchmark the intracardiac electrogram signal quality compared to commercially available systems in patients undergoing assessment and ablation of cardiac arrhythmias. |
| **Study Design** | A prospective, multi-center, open-label, single-arm study to evaluate the safety and technical performance of the CathVision ECGenius® system.<br>Patients who are scheduled to undergo an EP procedure and meet the inclusion/exclusion criteria will be enrolled in the study. Intracardiac signals will be passively recorded using CathVision ECGenius® System in parallel with the commercial EP recording system. |
| **Sample size** | Up to 30 subjects shall be enrolled in the study. |
| **Investigational Sites** | Up to two (2) investigational sites in the United States. |
| **Study Duration / Follow-up Period** | Study enrollment is planned for 1-3 months. |

| | |
|---|---|
| **Primary Endpoint** | The Primary endpoint of the study will be evaluated as the safety and technical success of CathVision ECGenius® System to collect and record intracardiac signals during EP procedures. With focus on:<br>• To record and plot low voltage electrograms<br>• To assess the improved signal (better signal to noise ratio) compared with the standard signal<br>• To visualize the shape and timing of electrograms |
| **Secondary Endpoint** | The Secondary endpoint of the study will be evaluated as the technical performance of CathVision ECGenius® System during routine EP procedures.<br>• To log time stamp for arrhythmia termination when termination is successful<br>• To confirm compatibility of CathVision ECGenius® system with commercially available 3D mapping systems and with available intracardiac catheters.<br>• To have no or minimal device malfunctions reported with the use of the CathVision ECGenius® |
| **Entry Criteria** | Inclusion Criteria<br>Eligible subjects will meet ALL the following inclusion criteria:<br>1. Patient is scheduled for catheter ablation or diagnostic electrophysiology procedure.<br>2. At least 18 years of age.<br>3. Able and willing to provide informed consent or obtain consent from a legally authorized representative (LAR).<br>Exclusion Criteria<br>Eligible subjects will not meet ANY of the following exclusion criteria:<br>1. Patient inability to understand or refusal to sign informed consent.<br>2. Patient is a prisoner or under incarceration<br>3. Patients who in the opinion of the physician are not candidates for this study. |

## Table of Contents

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# 1. Purpose

To define the use of statistical techniques in the evaluation and control of product and processes in order to ensure, with a high degree of confidence, that all products and processes meet requirements.

# 2. Scope

This document provides insight into the use of a series of characterization techniques. This procedure is applicable to all processes and operations which require the use of statistical rationales.

# 3. Definitions

None

# 4. Responsibilities

CathVision Clinical – responsible for determining the appropriate statistical techniques and rationale to be used for activities that require data analysis and determination of sampling sizes
CathVision Quality – responsible for reviewing the adequacy and appropriateness of the statistical techniques and sampling plans used in design verification and validation testing, process validations, and test protocols.

# 5. Procedure

## 5.1. Inclusions

Potential subjects must meet ALL of the following criteria to be eligible for inclusion in the study:

1. Patient is scheduled for catheter ablation or diagnostic electrophysiology procedure.
2. At least 18 years of age.
3. Able and willing to provide informed consent or obtain consent from a legally authorized representative (LAR).

## 5.2. Exclusions

1. Patient inability to understand or refusal to sign informed consent.
2. Patient is a prisoner or under incarceration
3. Patients who in the opinion of the physician are not candidates for this study.

## 5.3. Primary safety endpoints

Freedom from major adverse events, evaluated at hospital discharge.

## 5.4. Primary performance endpoints

The Primary Performance endpoint of study will be evaluated as technical success of CathVision ECGenius™ System to collect and record intracardiac signals during EP procedures. With focus on:

- To record and plot low voltage electrograms
- To assess the improved signal (better signal to noise ratio) compared with the standard signal
- To visualize the shape and timing of electrograms

## 5.5. Sample Size

The sample size of 30 is reached by analyzing similar trials in the same field, see the table below where the average sample size is 30 across three comparable trials. Source: Clinicaltrials.gov

| Study title | Sample size | Location | Sponsor |
|---|---|---|---|
| Novel Cardiac Signal Processing System for Electrophysiology Procedures | **30** | Mayo Clinic Texas and Florida | Biosig Technologies Inc. |
| Clinical Utility and Validation of the Rhythmia Mapping System for the Treatment of Cardiac Arrhythmia | **20** | Beth Israel Deaconness, Boston | Beth Israel Deaconness, Boston |
| Feasibility Study of the FARAPULSE Endocardial Multi Ablation System in the Treatment of Persistent Atrial Fibrillation (PersAFOne) | **40** | Na Homolka, Prague and University Hospital of Split | Farapulse Inc. |

## 5.6. Statistical analysis

| Endpoint | Statistical method | Hypothesis & benchmark |
|---|---|---|
| Freedom from major adverse events, evaluated at hospital discharge. | • Count number of AEs<br>• Percentage: [Procedures with AE] / [Total number of procedures] | • 3.5% of patients develop major AE within 30 days of procedure.<br>• Zero CathVision Cube-related AE are expected. |
| Recording low-voltage electrograms | • Count number of low-voltage electrograms plotted in total<br>• Percentage: [Total number low-voltage electrogram plots] / [Total number of procedures)<br>• Physician user quantitatively score low-voltage electrogram plots on “ease” of interpretation of EGMs” [0-5] on CathVision Cube and on existing EP system<br>o 0: Impossible<br>o 1: Very difficult | • At least one low-voltage electrogram plot per procedure<br>• CathVision not inferior to existing EP recording system |

| Endpoint | Statistical method | Hypothesis & benchmark |
|---|---|---|
| | ○ 2: Difficult<br>○ 3: Possible<br>○ 4: Easy<br>○ 5: Very easy<br>• Average physician score on CathVision ECGenius™ vs average physican score on existing EP system | |
| Assessing the improved signal quality (baseline noise level peak-to-peak) | • Peak-to-peak amplitude of baseline noise, on unipolar electrogram, at at least 1 site with low-voltage electrograms, and averaged if more than 1.<br>• Peak-to-peak amplitude of baseline noise, on bipolar electrogram, at at least 1 site with low-voltage electrograms, and averaged if more than 1.<br>• Non-inferior peak-to-peak amplitude of baseline noise to existing EP recording system. | • Hypothesis is below 50uV unipolar baseline noise peak-to-peak<br>• Hypothesis is below 20uV bipolar baseline noise peak-to-peak<br>• Hypothesis is non-inferior to existing EP recording system. |
| To visualize the shape and timing of electrograms | • Record activation timing with respect to surface ecg<br>• Classify morphology | Exploratory so no specific hypothesis |

# 6. References to CathVision SOPs

- SOP-00023 Clinical Evaluation v1
- SOP-00180 CRO Management v1